

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

To:

DU PONT PHARCEUTICALS
COMPANY
Attn. O'BRIEN, M.
Legal/Patent Records Center
1007 Market Street
Wilmington, Delaware 19898
UNITED STATES OF AMERICA

Date of mailing
(day/month/year)

01/09/1999

Applicant's or agent's file reference

DM6919

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/US 99/00747

International filing date

(day/month/year)

14/01/1999

Applicant

DU PONT PHARMACEUTICALS COMPANY

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

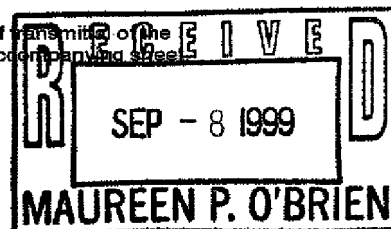
Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.



2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Claudia Aragone

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference DM6919	FOR FURTHER ACTION <small>see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.</small>	
International application No. PCT/US 99/ 00747	International filing date (<i>day/month/year</i>) 14/01/1999	(Earliest) Priority Date (<i>day/month/year</i>) 14/01/1998
Applicant DU PONT PHARMACEUTICALS COMPANY		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

PREPARATION OF A LIPID BLEND AND A PHOSPHOLIPID SUSPENSION CONTAINING THE LIPID BLEND, AND CONTRAST AGENTS BASED ON THESE

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

international application No.
PCT/US 99/00747

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 1-44 in part
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-23 in part, and 36-44

The process for preparing a phospholipid suspension as described in claims 1-23, and the phospholipid suspension thus obtained.

2. Claims: 1-23 in part, and 24-28

The process for preparing a perfluorocarbon-containing contrast agent according to these claims.

3. Claims: 29-35

The process for the prepreparation of a lipid blend according to these claims.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-44 in part

In view of the large number of compositions, which are defined by the general definition in the claims, the search had to be restricted for economic reasons. The search was limited to the compositions for which pharmacological data was given and/or the compositions mentioned in the claims, and to the general idea underlying the application (see guidelines, Chapter III, paragraph 2.3).

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/00747

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 6 A61K9/127 A61K49/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 0 349 429 A (CENTRE NAT RECH SCIENT) 3 January 1990 (1990-01-03) examples claim 1	1-28, 36-44
Y	US 5 637 289 A (KLAVENESS JO ET AL) 10 June 1997 (1997-06-10) example 5	1-28, 36-44
Y	WO 95 32006 A (IMARX PHARMACEUTICAL CORP) 30 November 1995 (1995-11-30)	1-28
X	examples 1-3	36-44
P,Y	WO 98 47487 A (DUMEX LTD AS ;NIELSEN LISE SYLVEST (DK)) 29 October 1998 (1998-10-29) page 66 - page 67	1-28
P,X		1,17-23
	--- -/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

12 August 1999

Date of mailing of the international search report

01.09.99

Name and mailing address of the ISA

European Patent Office, P.B. 5616 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Dullaart, A

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/00747

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 96 31196 A (IMARX PHARMACEUTICAL CORP) 10 October 1996 (1996-10-10)	1-35
X	example 1 ---	36-44
Y	G. GREGODIADIS (EDITOR): "Liposome Technology, Volume 1: Preparation of liposomes" 1984, CRC PRESS, INC., BOCA RATON, US XP002101586 13391 page 29 - page 35 & D.W. DEAMER: "PREPARATION OF SOLVENT VAPORIZATION LIPOSOMES" ---	1-23
Y	OHKI K ET AL: "SHORT AND LONG RANGE CALCIUM-INDUCED LATERAL PHASE SEPARATIONS IN TERNARY MIXTURES OF PHOSPHATIDIC ACID PHOSPHATIDYLCHOLINE AND PHOSPHATIDYLETHANOLAMINE" CHEMISTRY AND PHYSICS OF LIPIDS, 1989, VOL. 50, NO. 2, PAGE(S) 109-118., XP002101581	1-44
X	abstract page 110, left-hand column page 113; figure 4 page 117 ---	36-44
A	MARUYAMA KAZUO ET AL.: "Prolonged circulation time in vivo of large unilamellar liposomes composed of distearoyl phosphatidylcholine and cholesterol containing amphipathic poly(ethylene glycol)." BIOCHIMICA ET BIOPHYSICA ACTA, 1992, VOL. 1128, PAGES 44-49, XP002101582 table 1 figures 1-3 ---	1-28, 36-44
A	BEDU-ADDU FK ET AL: "Effects of polyethyleneglycol chain length and phospholipid acyl chain composition on the interaction of polyethyleneglycol-phospholipid conjugates with phospholipid: implications in liposomal drug delivery." PHARM RES, MAY 1996, VOL. 13, NO. 5, PAGE(S) 710-717, XP002101583 paragraph 'RESULTS! --- -/--	1-28, 36-44

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/00747

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A,P	BELSITO S. ET AL: "Sterically stabilized liposomes of DPPC/DPPE-PEG:2000. A spin label ESR and spectrophotometric study" BIOPHYSICAL CHEMISTRY, 5-10-1998, VOL. 75, NO. 1, PAGE(S) 33-43, XP002101584 figure 1	1-28, 36-44
Y,P	figures 5,6; table 2 ---	29-35
A	NIKOLOVA AN ET AL: "Effect of grafted PEG-2000 on the size and permeability of vesicles." BIOCHIM BIOPHYS ACTA, 22-11-1996, VOL. 1304, NO. 2, PAGE(S) 120-128, XP002101585 the whole document ---	1-23, 36-44
Y	WO 96 08234 A (IMARX PHARMACEUTICAL CORP) 21 March 1996 (1996-03-21) ---	1-28
X	examples	36-44
P,Y	WO 98 10799 A (IMARX PHARMACEUTICAL CORP) 19 March 1998 (1998-03-19) ---	1-28
P,X	example 1	36-44
Y	WO 96 40285 A (IMARX PHARMACEUTICAL CORP ;UNGER EVAN C (US); SHEN DEKANG (US); WU) 19 December 1996 (1996-12-19) ---	1-28
X	example 6	36-44
P,Y	WO 98 51284 A (IMARX PHARMACEUTICAL CORP) 19 November 1998 (1998-11-19) ---	1-28
P,X	example 12	36-44
Y	WO 97 40858 A (IMARX PHARMACEUTICAL CORP) 6 November 1997 (1997-11-06) ---	1-28
X	examples	36-44
Y	WO 95 15118 A (MATSUNAGA TERRY ;UNGER EVAN C (US); YELLOWHAIR DAVID (US)) 8 June 1995 (1995-06-08) ---	1-28
X	page 25 examples claims 19,20 ---	29-44
E	EP 0 901 793 A (IMARX PHARMACEUTICAL CORP) 17 March 1999 (1999-03-17) examples 1,2 -----	1-28, 36-44

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/00747

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0349429	A	03-01-1990	FR 2634375 A	26-01-1990
			AT 85888 T	15-03-1993
			DE 68904999 T	12-06-1997
			ES 2054053 T	01-08-1994
			GR 3007265 T	30-07-1993
			GR 3022121 T	31-03-1997
			JP 2118858 C	06-12-1996
			JP 2149336 A	07-06-1990
			JP 8024840 B	13-03-1996
			KR 9614869 B	21-10-1996
			US 5174930 A	29-12-1992

US 5637289	A	10-06-1997	AU 676148 B	06-03-1997
			AU 3348593 A	03-08-1993
			EP 0620745 A	26-10-1994
			FI 943264 A	04-08-1994
			JP 7505137 T	08-06-1995
			NO 942562 A	07-07-1994
			AT 168564 T	15-08-1998
			AU 676146 B	06-03-1997
			AU 3348393 A	03-08-1993
			CA 2127704 A	22-07-1993
			DE 69319888 D	27-08-1998
			DE 69319888 T	11-02-1999
			WO 9313802 A	22-07-1993
			EP 0620743 A	26-10-1994
			ES 2120493 T	01-11-1998
			JP 7505135 T	08-06-1995
			NO 942560 A	07-07-1994
			US 5567412 A	22-10-1996
			US 5614169 A	25-03-1997

WO 9532006	A	30-11-1995	US 5874062 A	23-02-1999
			AU 700799 B	14-01-1999
			AU 2601395 A	18-12-1995
			AU 2645495 A	18-12-1995
			CA 2191079 A	30-11-1995
			CN 1160357 A	24-09-1997
			CN 1149259 A	07-05-1997
			EP 0760684 A	12-03-1997
			EP 0762899 A	19-03-1997
			JP 10500691 T	20-01-1998
			JP 10500692 T	20-01-1998
			WO 9532005 A	30-11-1995
			US 5736121 A	07-04-1999

WO 9847487	A	29-10-1998	AU 6919598 A	13-11-1998

WO 9631196	A	10-10-1996	US 5705187 A	06-01-1998
			AU 5375596 A	23-10-1996
			BR 9604786 A	07-07-1998
			CA 2217494 A	10-10-1996
			EP 0818989 A	21-01-1998

WO 9608234	A	21-03-1996	US 5773024 A	30-06-1998
			AU 2185095 A	19-06-1995
			AU 3146595 A	29-03-1996
			BR 9509011 A	30-09-1997

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/00747

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9608234 A		CA 2177713 A	08-06-1995
		CA 2200061 A	21-03-1996
		CN 1158082 A	27-08-1997
		EP 0740528 A	06-11-1996
		EP 0788348 A	13-08-1997
		JP 10505900 T	09-06-1998
		JP 9506098 T	17-06-1997
		WO 9515118 A	08-06-1995
		US 5733572 A	31-03-1998
		US 5922304 A	13-07-1999
		US 5705187 A	06-01-1998
		US 5656211 A	12-08-1997

WO 9810799 A	19-03-1998	AU 4089897 A	02-04-1998
		AU 4235697 A	02-04-1998
		WO 9810798 A	19-03-1998
		US 5846517 A	08-12-1998

WO 9640285 A	19-12-1996	AU 6270396 A	30-12-1996
		CA 2218541 A	19-12-1996
		EP 0831932 A	01-04-1998

WO 9851284 A	19-11-1998	AU 7378798 A	08-12-1998
		AU 7796198 A	08-12-1998
		WO 9851282 A	19-11-1998

WO 9740858 A	06-11-1997	US 5776429 A	07-07-1998
		AU 2451097 A	19-11-1997
		CN 1216925 A	19-05-1999
		EP 0923383 A	23-06-1999

WO 9515118 A	08-06-1995	US 5585112 A	17-12-1996
		US 5542935 A	06-08-1996
		US 5773024 A	30-06-1998
		US 5733572 A	31-03-1998
		AU 1004399 A	04-03-1999
		AU 2185095 A	19-06-1995
		AU 696056 B	27-08-1998
		AU 6953794 A	03-01-1995
		AU 683900 B	27-11-1997
		AU 7043194 A	03-01-1995
		AU 8840698 A	04-02-1999
		CA 2164846 A	22-12-1994
		CA 2177713 A	08-06-1995
		CN 1137748 A	11-12-1996
		EP 0802788 A	29-10-1997
		EP 0712293 A	22-05-1996
		EP 0740528 A	06-11-1996
		JP 8511523 T	03-12-1996
		JP 8511526 T	03-12-1996
		JP 9506098 T	17-06-1997
		WO 9428874 A	22-12-1994
		WO 9428780 A	22-12-1998
		US 5922304 A	13-07-1999
		US 5705187 A	06-01-1998
		US 5853752 A	29-12-1998
		US 5656211 A	12-08-1997
		US 5776429 A	07-07-1998

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/00747

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9515118 A		CN 1125389 A	26-06-1996
		CN 1125393 A	26-06-1996
		AU 3146595 A	29-03-1996
		BR 9509011 A	30-09-1997
		CA 2200061 A	21-03-1996
		CN 1158082 A	27-08-1997
		EP 0788348 A	13-08-1997
		JP 10505900 T	09-06-1998
		WO 9608234 A	21-03-1996

EP 0901793 A	17-03-1999	NONE	
